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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/518,381	03/03/2000	Yi Li	1488.1220002/EKS/EJH	5756

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EXAMINER	
BASI, NIRMAL SINGH	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 09/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/518,381	LI ET AL.	
	Examiner	Art Unit	
	Nirmal S. Basi	1646	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 27 August 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will not be entered because:

   (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *23-29,31,33-39,41,43-49,51,53-61,65-73,75,77-81 and 83*.

   Claim(s) withdrawn from consideration: *30,32,40,42,50,52,62,64,74,76,82 and 84-96*.

8. ☐ The drawing correction filed on *03 March 2000* is a)☒ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

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Continuation of 2. NOTE: Newly added claims and amended claims would require a new search and raise new 35 USC 1st paragraph issues.

Continuation of 5. does NOT place the application in condition for allowance because: Applicants amendments and arguments do not overcome the rejections, of record, under 35 U.S.C. 101 and 112. The claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for reasons of record. The polynucleotides of SEQ ID NO:3 has not been shown to be a marker for cancer. The use of EDG-1-1ike G-protein coupled receptor molecules to treat and/or diagnose, for example, cancer, is claimed to be a substantial utility as it provides a benefit to the public. There is no clear nexus between the G-protein coupled receptor (EDG-1-like) and cancer which is disclosed in the speciffcation or prior art. Further the postfiling art of Van Brocklyn does not disclose EDG-I-like G protein coupled receptor is a marker for cancer. At the time of filing instant Application, the specification nor prior art supported the assertion that antagonists of the EDG-I-like G protein coupled receptor could be used to treat cancer or the polynucleotides of the invention could be used for the detection of cancer. The functionality of claimed EDG-I-like G protein coupled receptor was unknown. The utilities disclosed in the specification are based on methods of using receptor polypeptides and polynucleotides as a target for diagnosis and treatment of disorders and for drug-screening. EDG-I-like G protein coupled receptor is found in a variety of tissue. In light of the specification the skilled artisan can speculate that EDG-I-like G protein coupled receptor is a seven transmembrane protein belonging to the G-protein coupled receptor super family. However, no disclosure is provided within the instant specification on what specific function a putative EDG-I-like G protein coupled receptor possesses, or how to specifically assay for such, ligands that bind, promoters that activate, nor are any disease states disclosed that are directly related to EDG-I-like G protein coupled receptor dysfunction. There is no disclosure in the specification of ligands that bind to EBI-1 receptor or EDG-I-like G protein coupled receptor. The divergent nature and ligand specificity of G protein coupled receptors was disclosed in the previous Office Action (see Mudroch et al, Watson et al). The utility of EDG-I-like G protein coupled receptor cannot be implicated solely from homology to known G-protein coupled receptors because the art does not provide teaching stating that all members of a sub-family of G-protein coupled receptors must have the same effects, the same ligands and be involved in the same disease states, the art discloses evidence to the contrary. The EDG-I-like G protein coupled receptor of instant invention is considered by the examiner to be a member of the orphan receptor of G-protein coupled receptors i.e. seven transmembrane receptor with no known endogenous ligands. The specification compares claimed receptor to EDG-1 receptor of SEQ ID NO:18, which itself is an orphan receptor without a function. The receptor of SEQ ID NO:18 can not be used to infer a function on claimed EDG-I-like G protein coupled receptor because all G protein coupled receptors do not have the same function or ligand specificity . There is no evidence of record or any line of reasoning that would support a conclusion that the claimed receptor of the instant application was, as of the filing date, useful for diagnosis, prevention, and treatment of disease, such as cancers etc. Until some actual and specific significance can be attributed to the protein SEQ ID NO:4, or the gene encoding it, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. The DNA of the instant invention and the protein encoded thereby are compounds, which share some structural similarity to receptor proteins having GPCR domains based on sequence similarity. As disclosed by the specification, the family of proteins related to EDG-1 receptor may have diverse effects and bind a diverse number of ligands. The family of proteins having GPCR like domains has different levels of expression, and play roles in the pathogenesis of various diseases. Although the family of receptor proteins having EDG receptor like domains may share some common structural motifs, various members of the family may have different sites of action and different biological effects. In the absence of knowledge of the ligand for EDG-I-like G protein coupled receptor or the biological significance of this protein, there is no immediately evident patentable use. To employ a protein of the instant invention in any of the disclosed methods would clearly be using it as the object of further research. Such a use has been determined by the courts to be a utility, which, alone, does not support patentability. Post filing art further highlights the difficulty in assigning function to G protein-coupled receptors. As sated in a previous Office Action,Brocklyn discloses the EDG family of proteins is expressed in various tissues, have different ligand specificity and have different activities. EDG-1, EDG-3, and EDG-5 are spingosine-1-phospahte (SPP) receptors; EDG-2 and EDG-4 and EDG-7 are lysophosphatidic (LPPA) receptors. Applicant argues the EDG-1-like G protein and EDG-6 have the same function. Brocklyn discloses, before their publication (2000), it was unknown that EDG-6 was a receptor for SPP. Brocklyn also discloses that EDG-6 does not belong to either SPP or LPA subfamily of EDG receptors but it displays a similar degree of homology to all 5 of the previously identified members of the family. Therefore, Brocklyn argues away from prediction function based on homology to known proteins in a family. Further the post filing art of Kohno et al (Genes to Cell, Vol 8, No.8, August 2003, pages 685-697) discloses little is known about Edg-6. Kohno also discloses Edg-1/S1F1. Edg-3/S1P 3, Edg-s/SIP 2, Edg-6/S1P 4 and Edg-8/S1P 5, have been identified as specifc Sph-I-P receptors. The post filing art of Graler et al (Journal of Cellular Biochemistry, Vol. 89, pages 507-2003), also provided by Applicant, dislcoses upon stimulation, SIPl and SIP5 exert a negative effect on the level of cyclic AMP (cAMP) whereas bindingof S1P to S1P2 andS1P3 raise the CAMP level . With regard to phenotypical responses it has been demonstrated that S1P, and S1P3 induce cell migration towards an S1Pstimulus whereas S1P2 inhibits cell migration and membrane ruffling (page 508, column 1, pargragraphs 1 and 2). Therefore menbers of Edg family of proteins have been shown to have opposite effects and therfore can not be used to predict function or dysfunction of claimed receptor.

In conclusion , the utilities asserted by Applicant are not specific or substantial. Since no specific function of the polypeptide of instant invention is known, and the hypothesized function is based entirely on conjecture from homologous polypeptides, the asserted utilities are not specific to instant polypeptide, but rather are based on family attributes. Neither the specification nor the art of record disclose the protein of SEQ ID NO:4 or fragments thereof useful to identify drugs that affect said protein and modulate its activity. Since neither the specification nor the art of record disclose any activities or properties that would constitute a real world context of use for the claimed receptor and fragments thereof, further experimentation is necessary to attribute a utility to the claimed polypeptides and fragments thereof.

The claims also remain rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.